

Exhibit B

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Characteristics at Baseline by Cohort

	Nurses’ Health Study I n=81,869	Nurses’ Health Study II	Sister Study n=40,647	Women’s Health Initiative
Race				
White	79,895 (98)	59,101 (96)	35,483 (87)	61,292 (84)
Black	1,196 (1)	826 (1)	3,293 (8)	5,735 (8)
Other	778 (1)	1,334 (2)	1,853 (5)	6,033 (8)
Missing	0	0	18	207
Birth cohort^a				
1915-1929	28,308 (35)	0 (0)	2 (0)	27,178 (37)
1930-1944	49,961 (61)	6 (0)	10,701 (26)	42,886 (59)
1945-1959	3,600 (4)	52,907 (86)	22,681 (56)	3,203 (4)
1960-1971	0 (0)	8,348 (14)	7,2623 (18)	0 (0)
Education				
High school or less	0 (0)	0 (0)	5,898 (15)	15,310 (21)
Some college	0 (0)	0 (0)	13,245 (33)	26,192 (36)
Completed college	81,869 (100)	61,261 (100)	21,498 (53)	31,179 (43)
Missing	0	0	6	586
Body mass index (BMI; kg/m²)				
<25.0 (Normal)	52,290 (64)	25,970 (43)	16,726 (41)	30,421 (42)
25.0-29.9 (Overweight)	19,793 (24)	18,017 (30)	12,591 (31)	24,768 (34)
>30 (Obese)	9,653 (12)	16,665 (27)	11,319 (28)	17,905 (25)
Missing	133	609	11	173
Parity				
Nulliparous	4,414 (5)	10,462 (17)	7,523 (19)	9,092 (12)
1 birth	5,726 (7)	8,375 (14)	5,856 (14)	6,396 (9)
2 births	22,828 (28)	24,345 (40)	15,022 (37)	18,997 (26)
3 or more births	47,479 (59)	18,079 (30)	12,221 (30)	38,352 (53)
Missing	1,422	0	25	430
Smoking status				
Never smoker	35,825 (44)	39,999 (65)	23,034 (57)	36,791 (51)
Former smoker	23,749 (29)	18,319 (30)	14,333 (35)	30,994 (43)
Current smoker	22,151 (27)	2,872 (5)	3,271 (8)	4,593 (6)
Missing	144	71	9	889
Ever oral contraceptive use	40,816 (50)	52,484 (86)	34,310 (84)	29,890 (41)
Missing	11	0	32	1
Had tubal ligation	14,402 (18)	16,603 (27)	11,698 (29)	12,609 (17)
Missing	22	0	16	388
Had hysterectomy	14,171 (17)	8,463 (14)	6,868 (17)	20,063 (27)
Missing	3	0	23	70
Patent^b	54,087 (66)	39,012 (64)	24,310 (60)	43,037 (59)
Missing	21	0	35	289
Postmenopausal	34,228 (42)	54,795 (89)	23,987 (59)	73,267 (100)
Ever hormone therapy use	13,919 (17)	27,590 (45)	15,098 (37)	39,777 (54)
Missing	18	113	121	1

^aApproximation based on age at enrollment and median enrollment year; studies did not provide exact dates^bNo hysterectomy or tubal ligation

eTable 2. Characteristics at Baseline by Use of Powder in the Genital Area

	Never User of Powder n= 158,084	Ever User of Powder n= 98,960
Study		
Nurses' Health Study	48,429 (31)	33,440 (34)
Nurses' Health Study II	45,096 (29)	16,165 (16)
Sister Study	29,807 (19)	10,840 (11)
Women's Health Initiative	34,752 (22)	38,515 (39)
Race		
White	145,996 (92)	89,775 (91)
Black	5,151 (3)	5,899 (6)
Other	6,825 (4)	3,173 (3)
Education		
High school or less	12,234 (8)	8,974 (9)
Some college	21,672 (14)	17,765 (18)
Completed college	123,880 (79)	71,927 (73)
Body Mass Index (BMI; kg/m²)		
<25.0 (Normal)	82,681 (53)	42,726 (43)
25.0-29.9 (Overweight)	45,186 (29)	29,983 (30)
≥30 (Obese)	29,630 (19)	25,912 (26)
Parity		
Nulliparous	20,153 (13)	11,338 (12)
1 birth	16,690 (11)	9,663 (10)
2 births	51,328 (33)	29,864 (30)
3 or more births	68,863 (44)	47,268 (48)
Smoking status		
Never smoker	85,855 (55)	49,794 (51)
Former smoker	51,003 (32)	36,392 (37)
Current smoker	20,666 (13)	12,221 (12)
Ever oral contraceptive use	101,189 (64)	56,311 (57)
Had tubal ligation	34,717 (22)	20,595 (21)
Had hysterectomy	28,072 (18)	21,493 (22)
Patent	100,245 (63)	60,201 (61)
Postmenopausal	112,354 (71)	73,923 (75)
Ever hormone therapy use	57,768 (37)	38,616 (39)

Missing: Race (112 unexposed, 113 exposed), Education (298 unexposed, 294 exposed), BMI (587 unexposed, 339 exposed), Parity (1,050 unexposed, 827 exposed), Smoking status (560 unexposed, 533 exposed), Oral contraceptive use (34 unexposed, 10 exposed), Tubal ligation (193 unexposed, 233 exposed), Hysterectomy (56 unexposed, 40 exposed), Patent (168 unexposed, 177 exposed), Hormone therapy use (178 unexposed, 75 exposed)

eTable 3. Stratified Pooled Hazard Ratios (HRs) and 95% (CIs) for the Association Between Long-Term or Frequent Use of Powder in the Genital Area and Risk of Ovarian Cancer

	Long-term use ^a HR (95% CI)	Heterogeneity p-value	Frequent use ^a HR (95% CI)	Heterogeneity p-value
Age at baseline				
<60	1.13 (0.80, 1.60)	0.74	1.08 (0.95, 1.23)	0.62
≥60	0.96 (0.74, 1.25)		1.18 (0.82, 1.71)	
Race				
Non-Hispanic White	0.99 (0.80, 1.23)	0.52	1.08 (0.96, 1.22)	0.51
Other	1.26 (0.65, 2.45)		1.32 (0.63, 2.76)	
Menopausal status^b				
Premenopausal	NE ^c	NE ^c	1.07 (0.72, 1.57)	0.98
Postmenopausal	1.04 (0.84, 1.28)		1.10 (0.96, 1.24)	
Follow-up time				
0-10 years	1.08 (0.84, 1.39)	0.57	1.15 (0.93, 1.41)	0.69
>10 years	0.89 (0.61, 1.29)		1.06 (0.92, 1.24)	
Hormone therapy use^d				
Never	1.03 (0.74, 1.43)	0.68	1.01 (0.80, 1.27)	0.39
Ever	1.07 (0.81, 1.41)		1.24 (0.97, 1.59)	
BMI				
<30 kg/m ²	1.00 (0.78, 1.28)	0.86	1.12 (0.99, 1.28)	0.39
≥30 kg/m ²	1.02 (0.70, 1.47)		0.90 (0.67, 1.20)	
Parity				
Nulliparous	0.59 (0.32, 1.12)	0.21	1.04 (0.70, 1.55)	0.51
Parous	1.10 (0.88, 1.37)		1.10 (0.97, 1.25)	
Hysterectomy				
No	1.00 (0.78, 1.28)	0.94	1.12 (0.98, 1.28)	0.75
Yes	1.06 (0.73, 1.53)		1.00 (0.75, 1.31)	
Tubal ligation status				
No	0.98 (0.78, 1.24)	0.83	1.15 (1.01, 1.31)	0.06
Yes	1.16 (0.71, 1.88)		0.74 (0.52, 1.05)	
Patency				
Patent	1.00 (0.76, 1.32)	0.99	1.19 (1.03, 1.37)	0.15
Not patent	1.03 (0.75, 1.41)		0.91 (0.73, 1.14)	

Adjusted for study, race/ethnicity (white, African-American, other), education ≤high school, some college, ≥college graduate), BMI (as a restricted cubic spline), parity (0, 1, 2, 3+ births), ever oral contraceptive use, tubal ligation (yes/no), hysterectomy status (yes/no), menopausal status (pre or postmenopausal), ever hormone therapy use. Variables being stratified on were not included in the adjustment set.

^aReferent group = never users

^bMenopausal status updated throughout follow-up.

^cNot estimated due to low cell count for long-term exposed cases

^dAmong postmenopausal women only

eTable 4. Pooled Hazard Ratios and 95% CIs in Patent Women for Medically Confirmed Cases Overall and by Tumor Invasiveness, Location, and Histotype

	Number of cases ^a	Ever Use ^b (95% CI)	Long-term Use ^b (95% CI)	Frequent Use ^b (95% CI)
All medically-confirmed cases	1,182	1.10 (0.98, 1.24)	1.04 (0.78, 1.38)	1.17 (1.00, 1.38)
Invasiveness				
Invasive only	973	1.13 (0.99, 1.28)	1.14 (0.84, 1.55)	1.21 (1.02, 1.44)
Borderline	87	1.03 (0.68, 1.58)	1.19 (0.39, 3.65)	1.09 (0.61, 1.94)
<i>Heterogeneity p-value^c</i>		0.70	0.88	0.42
Tumor location				
Epithelial Ovarian	973	1.14 (1.00, 1.29)	1.10 (0.81, 1.49)	1.21 (1.02, 1.45)
Fallopian Tube	30	1.46 (0.71, 2.96)	3.61 (0.69, 18.8)	2.20 (0.94, 5.15)
Peritoneal	62	0.93 (0.56, 1.54)	1.38 (0.29, 6.47)	0.79 (0.41, 1.52)
<i>Heterogeneity p-value^c</i>		0.59	0.32	0.01
Histotype				
Serous	635	1.14 (0.97, 1.33)	1.08 (0.73, 1.60)	1.18 (0.95, 1.46)
Endometrioid	107	1.30 (0.88, 1.91)	1.32 (0.49, 3.53)	1.42 (0.86, 2.34)
Mucinous	67	1.02 (0.63, 1.66)	1.41 (0.49, 4.03)	1.37 (0.72, 2.60)
Clear Cell	53	1.35 (0.80, 2.31)	1.29 (0.36, 4.58)	1.17 (0.53, 2.57)
Other	229	1.03 (0.79, 1.35)	1.23 (0.66, 2.28)	1.08 (0.74, 1.56)
<i>Heterogeneity p-value^c</i>		0.82	0.96	0.93
Histotype II^d				
High grade serous	435	1.16 (0.96, 1.40)	1.06 (0.68, 1.66)	1.20 (0.91, 1.58)
Low grade serous	17	1.20 (0.48, 3.01)	1.00 (0.94, 1.06)	0.50 (0.11, 2.30)
Other	400	1.09 (0.89, 1.33)	1.21 (0.76, 1.91)	1.21 (0.92, 1.59)
<i>Heterogeneity p-value^c</i>		0.91	0.25	0.48

Other ovarian cancers not meeting the specified case definition were censored at time of diagnosis
Adjusted for study, race/ethnicity (white, black, other), education \leq high school, some college, \geq college graduate), BMI (as a restricted cubic spline), parity (0, 1, 2, 3+ births), duration of oral contraceptive use (never, 0-5 years, >5 years), menopausal status (pre or post-menopausal), duration of hormone therapy use (never, 0-5 years, >5 years).

^aFor ever use analysis; limited to women with complete covariate information

^bReferent group = Never users

^cFrom competing risks model: likelihood ratio test of model that allows effect estimate to vary by subtype compared to a model that does not

^dHigh grade serous defined as grade 2-4 serous or grade 3-4 endometrioid; Low grade serous = grade 1 serous

eAppendix. Questions Related to Use of Powder/Talc in the Genital Area in Each of the 4 Cohorts

Nurses' Health Study: 1982 questionnaire (underline in original questionnaire)

Have you ever commonly used talcum, baby powder or deodorizing powder to:

a. Apply to perineal (private) area?

Options: No; Daily; 1-6 times a week; less than once a week

b. Apply to sanitary napkins?

Options: No; Yes

Ever use defined as using ever on perineal area (a) or on sanitary napkins (b).

Frequent use defined as use on perineal area at least once per week. Participants who did not apply perineal talc but did apply talc to their sanitary napkins were considered to be non-frequent users for talc.

Long term use not assessed

Nurses' Health Study II: 2013 questionnaire (underline and CAPS in original questionnaire)

Have you ever used talcum, baby or deodorizing powder AT LEAST WEEKLY in the genital/rectal area or on sanitary napkins, tampons, or underwear?

Options: Never; Less than 1 year; 1 to <10 years; 10-<20 years; 20-<30 years; 30+ years

Ever use and **frequent use** defined as using at least weekly for any time period

Long-term use defined as using at least weekly for ≥ 20 years

Sister Study: Baseline Questionnaire (bold in original questionnaire)

During the ages of 10-13, about how often did you apply talcum powder to a **sanitary napkin, underwear, diaphragm, cervical cap, or directly to your vaginal area?** (*Mark one.*)

Options: Did not use; Sometimes; Frequently; Don't Know

In the past 12 months, how frequently have you applied talcum powder to a **sanitary napkin, underwear, diaphragm, cervical cap, or directly to your vaginal area?** (*Mark one.*)

Options: Did not use; Less than once a month; 1-3 times per month; 1-5 times per week; More than 5 times per month

In the past 12 months, what types of talcum powder have you usually used on a sanitary napkin, underwear, diaphragm, cervical cap, or your vaginal area? (*Mark all that apply.*)

Options: Did not use; Powder, Spray

Note: same questions were asked for talcum powder under arms and other parts of your body.

Ever use defined as use in 12 months prior to baseline or at ages 10-13.

Frequent use defined as use at least once per week (in the last 12 months) or "frequently" during ages 10-13.

Long-term use defined as perineal use at ages 10-13 and in the last 12 months.

Women who said they were non-users at one time point but who were missing data for the other were considered never users.

Women's Health Initiative: Observational Study Baseline Questionnaire

Have you ever used powder on your private parts (genital areas)?

Options: No; Yes

For how many years?

Options: Less than 1 year; 1-4 years; 5-9 years; 10-19 years; 20 or more years

Did you ever use a diaphragm (a birth control device that fits over the opening of your womb)?

Options: No, Yes

Did you ever use powder on your diaphragm?

Options: No; Yes

For how many years did you use powder on your diaphragm?

Options: Less than 1 year; 1-4 years; 5-9 years; 10-19 years; 20 or more years

Did you ever use powder on a sanitary napkin or pad?

Options: No; Yes

For how many years did you use powder on sanitary pads?

Options: Less than 1 year; 1-4 years; 5-9 years; 10-19 years; 20 or more years

Ever use defined as "Yes" to any of 3 'ever use' questions

Frequent use not assessed

Long term use defined as use for 20 or more years on any of 3 'years used' questions